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10/804,692	03/19/2004	Alexander Alekseevich Makarov	26114.14	9158
27683	7590	10/11/2005		
HAYNES AND BOONE, LLP 901 MAIN STREET, SUITE 3100 DALLAS, TX 75202			EXAMINER SOUW, BERNARD E	
			ART UNIT 2881	PAPER NUMBER

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/804,692

Applicant(s)

MAKAROV ET AL.

Examiner

Bernard E. Souw

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7, 10, 13, 16, 18-26, 41 and 49 is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 9, 11, 12, 14, 15, 17, 27-40, 42-48 and 50-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10/20/2004 + 10/29/04
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Information Disclosure Statement***

1. Receipt is acknowledged of information disclosure statements (IDS) submitted on 10/20/2004. The submission is in compliance with the provisions of 37 CFR 1.97.

Signed copies of the information disclosure statement are here enclosed.

### ***Preliminary Amendment***

2. The Preliminary Amendment filed 10/25/2004 has been entered.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 8, 11, 39, 40 and 43 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Franzen (USPAT 5,763,878).

Regarding claims 1, 8 and 39, Franzen discloses a tandem mass spectrometer as well as a method of operating the same, comprising an ion source 4, an ion trap 11 with a plurality of elongate electrodes 12, and a time of flight analyzer 19, as can be seen in Fig.1. Franzen's apparatus and method specifically comprises the step of trapping ions introduced from the ion source, and exciting the trapped ions so as to eject the said trapped ions substantially orthogonally with respect to the direction of

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elongation of the electrodes, such that the ejected ions travel to the collision cell; fragmenting ions introduced from the ion trap in the collision cell; ejecting fragmented ions from the collision cell such that they travel to the time of flight mass analyzer; and operating the time of flight mass analyzer to obtain a mass spectrum of ions therein. as recited in Col.4/ll.31-59, wherein a collision cell in the front portion of the time of flight mass used for ion fragmentation is recited in Col.6/line 67 and Col.7/ll.1-6 in reference to Fig.1, and further in Col.4/ll.63-67 and Col.5/ll.1-21 in reference to Figs.3 and 4.

► Regarding claim 2, Franzen applies an AC potential to the plurality of elongate electrodes, as recited in Col.4/ll.59-62 in reference of Fig.2.

► Regarding claims 11 and 40, Franzen's mass spectrometer includes a detector located adjacent tot the ion trap, as recited in Col.4/ll.10-16.

► Regarding claim 43, Franzen's time of flight mass spectrometer is of the orthogonal acceleration type, as recited in the Title and in the Abstract/lines 1-3.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 12, 14, 15, 17 and 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen.

Regarding claim 12, Franzen's ion detector intercepts a portion of the ejected ions orthogonally, as understood by one of ordinary skill in the art from Franzen's recitation in Col.4/ll.10-16.

Regarding claims 12, 14, 15, 17 and 27-33 operating the TOF to obtain a mass spectrum of fragmented ions is conventionally performed in a tandem ion trap + TOF mass spectrometer; so is also injecting a reference compound into the collision cell, and also the limitation of injecting and trapping ions having a broad  $m/z$  values, while ejecting ions of ions having a narrow range of  $m/z$  values, all these recited in Col.5/ll.16-67 and Col.6/ll.1-67.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to intercept the ejected ions also orthogonally by the detector, if the ions are already ejected from the trap orthogonally, as recited in Col.4/ll.10-16.

One of ordinary skill in the art would have been motivated to intercept the ejected ions also orthogonally by the detector, if the ions are already ejected from the trap orthogonally, since this is the most simple and natural way to detect the ions, or otherwise one would have to make special provisions in order to detect the ions not orthogonally, which only means additional work and expense.

It would have been further obvious to one of ordinary skill in the art at the time the invention was made to obtain a mass spectrum of fragmented ions in a tandem ion trap + TOF mass spectrometer as in Franzen's, which is specifically equipped with a collision cell to fragmentize the ions, as recited in Col.6/line 67, Col.7/ll.1-6, Col.4/ll.63-

67 and Col.5/II.1-21, since otherwise it does not make sense to only fragmentize the ions without the intent to measure the mass spectrum of the fragmentized ions.

One of ordinary skill in the art would have been motivated to obtain a mass spectrum of fragmented ions in a tandem ion trap is specifically equipped with a collision cell to fragmentize the ions, since this is just the purpose of adding a collision cell to the MS, as expressly taught by Franzen in Col.7/II.3-6.

6. Claims 3, 42 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen in view of Reinhold et al. (USPAT 6,483,109).

Franzen recites all the limitations of claims 3 and 42, except the recitation that the collision cell is of a planar design.

Reinhold et al. disclose an apparatus and method for trapping and fragmenting ions similar to Franzen's. Reinhold's collision cell is of a planar design, as shown in Fig.5C and recited in Col.13/II.39-42. As a consequence, Reinhold's trapped ions are ejected as a ribbon beam, as generally known in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the collision cell in a planar design, in order to save an extra step, as taught by Reinhold et al. in Col.13/II.37-39.

One of ordinary skill in the art would have been motivated to modify Franzen's tandem ion trap by adopting Reinhold's scheme (c) depicted in Fig.5C, since saving an extra step also means saving extra work and expense.

► Specifically regarding claim 44, Franzen's TOF mass analyzer is gridless, as understood by one of ordinary skill in the art from Franzen's Figs. 3 + 4. Similarly, Reinhold's TOF 35 shown in Fig.3A is also gridless, as understood by one of ordinary skill in the art.

It would have been an obvious matter of design choice to adopt Franzen's and/or Reinhold's type of TOF, since applicant has not disclosed that a gridless TOF would solve any stated problem or has any particular purpose and it appears that the invention would perform equally well with Franzen's and/or Reinhold's type of TOF. Therefore, Applicant's use of a specific gridless TOF that is typically different than Franzen's or Reinhold's is a mere matter of design choice that is unpatentable, because it only involves routine skill in the art.

7. Claims 34, 35, 38 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen in view of Reinhold et al.

Franzen as modified by Reinhold et al. recites all the limitations of claims 34, 35, 38 and 45, as previously applied to claims 1 and 39, but also including the use of a multiple selection/analysis stage including a plurality of fragmentation/analysis stage specifically recited by claims 34, 35, 38 and 45 in addition of the limitations of claims 3, 42 and 44 above. The specific limitation of a multiple selection/analysis stage including a plurality of fragmentation/analysis stage is taught by Reinhold et al., as recited in Col.5/ll.67-68, Col.6/ll.1-67, Col.7/ll.1-67 and Col.8/ll.1-40, wherein the recitation of the

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multiple generation of fragment ions up to the third generation (i.e., tertiary subset of precursor ions recited in claim 38) is expressly recited in Col.6/II.54-59.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a multiple selection/analysis stage including a plurality of fragmentation/analysis stage as taught by Reinhold et al., since the sampling procedure allows unambiguous identification of the  $m/z$  of the parent ion of a fragment even if all the ions of a particular  $m/z$  ratio are not selectively transferred, as taught by Reinhold et al. in Col.8/II.12-15.

One of ordinary skill in the art would have been motivated to modify Franzen's ion trap with fragmentation provision by Reinhold's multistage fragmentation, since such a multistage fragmentation offers a highly selective ion fragmentation, as taught by Reinhold et al. in Col.6/II.38-41.

► Still regarding claim 35, it would have been an obvious matter of design choice to eject tertiary subsets of precursor ions as pulses with any temporal widths as conducted by Franzen and/or Reinhold, since applicant has not disclosed that a temporal width of 10 ms would solve any stated problem or has any particular purpose and it appears that the invention would perform equally well with Franzen's and/or Reinhold's pulse temporal widths. Therefore, Applicant's use of a temporal width of 10 ms is a mere matter of design choice that is unpatentable, because it only involves routine skill in the art.



8. Claims 4-6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen in view of Bier et al. (USPAT 5,420,425).

► Franzen recites all the limitations of claims 4-6, 9 and 10, except the recitation of operating the collision cell to trap the ions.

Regarding claim 4, Bier et al. disclose an apparatus and method for trapping and fragmenting ions similar to Franzen's. Bier's ion trap comprises also a collision cell that is operated to trap the ions, as recited in Col.5/II.48-66, more specifically in Col.5/II.61-66.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the fragmentizing collisions also within the ion-trapping chamber, i.e., by ejecting the undesired ions, instead of ejecting the desired ions into an additional collision cell, since this saves an extra step and an extra chamber.

One of ordinary skill in the art would have been motivated to modify Franzen's ion trapping & fragmentizing method by Bier's method of fragmentizing the ions while they are being trapped, since saving extra step also means saving extra work and material.

- Regarding claim 5, the use of DC potential to trap the ions is recited by Franzen in Col.7/II.55-59 as well as by Bier et al. in Col.5/II.54-59.
- Regarding claim 6, the limitation of operating the collision cell using the DC potential only is recited by Bier et al. in Col.14/II.23-38.
- Regarding claim 9, Bier's collision cell comprises a plurality of elongated, composite rods having at least two parts, as recited in Col.9/II.58-68 and Col.10/II.1-63

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in reference to Figs. 2A-B-C, with a supplemental provision to convert the trap into collision cell, as recited in Col.5/ll.48-66. As shown in Figs.7A,B, Bier's ion trap & collision cell 701 comprises a plurality of elongate, composite rod electrodes having at least two parts, 715/717 and 716/718, to which an RF potential is applied to both parts 715/717 and 716/718, and a different DC potential is also applied to each part, as recited in Col.14/ll.39-57 regarding the AC/RF voltage, and in Col.14/ll.23-38 regarding the DC voltage, wherein the outputs of Fig.7A are connected to the inputs of Fig.7B, e.g., the output from RF amplifier 768 in Fig.7A to input transformer 755/767 to be applied to part 718/716 of the trap/collision cell.

9. Claims 36 and 37 recite parts and combinations of claims 27-33 previously rejected as being obvious over Franzen. Therefore, claims 36 and 37 are also rejected as being obvious over Franzen, but now with Reinhold et al. as a secondary prior art because of their dependencies, either directly or indirectly, on claim 34..

10. Claims 47 and 48 recite the same limitations as claims 11 and 40 previously rejected under 35 U.S.C. 102(b) as being clearly anticipated by Franzen. Therefore, claims 47 and 48 are also rejected as being obvious Franzen, but now with Reinhold as secondary prior art under 35 U.S.C. 103(a) because of their dependencies, either directly or indirectly, on claim 45.

11. Claim 50 recites the same limitations as claim 1 previously rejected under 35 U.S.C. 102(b) as being clearly anticipated by Franzen. Therefore, claim 50 is also rejected as being obvious Franzen, but now with Reinhold as secondary prior art under 35 U.S.C. 103(a) because of their dependencies, either directly or indirectly, on claim 45.

12. Claim 51 recites the same limitations as claims 3, 42 previously rejected under 102(b) as being clearly anticipated by Franzen. Therefore, claim 51 is also rejected as being obvious Franzen, but now with Reinhold as secondary prior art under 103(a), because of their dependencies, either directly or indirectly, on claim 45.

13. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen in view of Reinhold et al. and further in view of Schwartz et al. (USPAT 6,797,950).

Franzen as modified by Reinhold et al. shows all the limitations of claim 46, as previously applied to the parent claim 45, except the recitation that the exit aperture of the trap/storage is elongated like the electrodes.

Schwartz et al. disclose an apparatus and method for trapping and fragmenting ions similar to Franzen's. Schwartz's exit aperture 12 of the trap/storage 11 is elongated just like the electrodes, as can be seen in Fig.1 and recited in Col.1/ll.55-67 and Col.1/ll.1-3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the exit aperture of the trap/storage elongated just like the

electrodes, as taught by Schwartz et al., in order to make an efficient ejection of the trapped ions.

One of ordinary skill in the art would have been motivated to modify Franzen's ion trap by Schwartz's elongated ion exit aperture, since the resulting efficiency of ion injection into the TOF mass analyzer effectively increases the signal to noise ratio in the subsequent ion mass measurement.

14. Claims 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen in view of Reinhold and further in view of Bier et al.

Franzen as modified by Reinhold et al. shows all the limitations of claims 52 and 53, as previously applied to the parent claims 45-48-50, except the recitation that the collision cell comprises a plurality of elongated, composite rods having at least two parts.

Bier et al. disclose an apparatus and method for trapping and fragmenting ions similar to Franzen's and Reinhold's. Bier's collision cell comprises a plurality of elongated, composite rods having at least two parts, as recited in Col.9/ll.58-68 and Col.10/ll.1-63 in reference to Figs. 2A-B-C, with a supplemental provision to convert the trap into collision cell, as recited in Col.5/ll.48-66.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the fragmentizing collisions also within the ion trapping chamber, i.e., by ejecting the undesired ions, instead of ejecting the desired ions into an additional collision cell, since this saves an extra step and an extra chamber.

One of ordinary skill in the art would have been motivated to modify Franzen's ion trapping & fragmentizing method by Bier's method of fragmentizing the ions while they are being trapped, since saving extra step also means saving extra work and material.

Regarding claim 53, the two parts of Bier's composite rods are connected to separate power supplies. As shown in Fig.7B, specifically the first part 715/717 of trap 701 is connected to transformer 756/770, whereas the second part 716/718 is connected to transformer 755/767, as recited in Col.14/ll.26-38.

***Indication of Allowable Subject Matter***

15. Claims 7, 10, 13, 16, 18-26, 41 and 49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Reasons for Indication of Allowable Subject Matter***

16. The following is a statement of reasons for the indication of allowable subject matter:

► Claim 7 contains allowable subject matter, for reciting a method of operating a mass spectrometer comprising the provision of an electric field along the collision cell in which the gradient of the electric field monotonously increases along the ion path inside the collision cell, which is a limitation that has neither been anticipated nor rendered obvious by any prior art.

► Claim 10 contains allowable subject matter, for reciting the application of a DC potential to a pair of electrodes that sandwiches the composite rods, which can only be interpreted in the light of the specification, and hence, unique to Applicant's invention, while not being anticipated or rendered obvious by any prior art.

► Claims 13, 41 and 49 contain an allowable subject matter, for reciting that the ion detector and the collision cell are positioned on opposing sides of the ion trap, which is a limitation that has neither been anticipated nor rendered obvious by any prior art.

► Claims 16 and 26 contain an allowable subject matter, for reciting the step of filling the ion trap within an ion abundance determined using automatic gain control, which is again a limitation that has neither been anticipated nor rendered obvious by any prior art.

► Claims 18 contains an allowable subject matter, for reciting a method of operating a mass spectrometer, wherein the ion trap is a composite ion trap comprising first and second trapping regions arranged substantially co-axially along a common axis defining an ion path through the first trapping region and into the second trapping region; introducing ions generated by an ion source having the relatively broad range of  $m/z$  values into the first trapping region along the ion path; operating the first trapping region to trap ions across substantially all the relatively broad range introduced from the ion source and to eject ions within an intermediate range of  $m/z$  values axially thereby to travel to the second trapping region along the ion path; and operating the second trapping region to trap ions introduced from the first trapping region and to eject ions

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within the relatively narrow range of m/z values orthogonally, the limitation having been neither anticipated nor rendered obvious by any prior art.

► Claims 19-25 contains an allowable subject matter, for being dependent, either directly or indirectly, on an allowable claim 18.

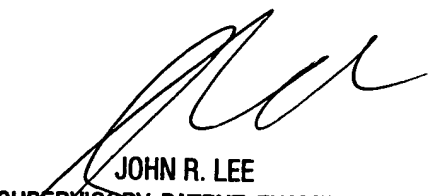
### ***Communications***

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard E Souw whose telephone number is 571 272 2482. The examiner can normally be reached on Monday thru Friday, 9:00 am to 5:00 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John R Lee can be reached on 571 272 2477. The central fax phone number for the organization where this application or proceeding is assigned is 571 273 8300 for regular communications as well as for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571 272 5993.

bes  
August 30, 2005

  
JOHN R. LEE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 2600